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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/842,930	04/25/2001	Paul H. Weigel	5820.603	1177

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EXAMINER
SPECTOR, LORRAINE

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

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APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.

EXAMINER

ART UNIT	PAPER NUMBER
	16

DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☒ Responsive to communication(s) filed on 2/13/63

☒ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 24, 28, 42, 88 is/are pending in the application.
Of the above, claim(s) 28 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☒ Claim(s) 24, 42, 88 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☒ Claim(s) 24, 28, 42, 88 are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

Part III: Detailed Office Action

Claims 24, 28, 42 and 88 are pending. The protein of SEQ ID NO:25 is a non-elected species, election having been made in paper number 11, without traverse. There being no generic claim, claim 28 stands withdrawn from prosecution.

Formal Matters:

Claims 42 and 88 are objected to for encompassing non-elected subject matter, there being no generic claim. Applicants are required to amend the claims to restrict the claimed subject matter to the elected species, SEQ ID NO:2.

The title of the invention remains objected to as being non-descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The claims are directed not to the identification of hyaluronic acid receptors, but to the receptors themselves.

Objections and Rejections under 35 U.S.C. §112:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24, 42 and 88 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for complete HARE 175, and fragments of HARE 175, is not enabling for HARE "comprising a sequence essentially as set forth in SEQ ID NO: 2".
The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims have been amended to recite that the claimed protein is one "comprising a

sequence essentially as set forth in SEQ ID NO: 2". Applicants have pointed the Examiner to paragraphs [0068]-[0071] of the specification for support for such. However, that portion of the specification defines "essentially as set forth" as meaning "that the sequence substantially corresponds to *at least a portion* of" the recited sequence, "and has relatively few amino acids which are not identical to, or a *biologically functional equivalent of,* the amino acids" of SEQ ID NO:2. The specification goes on to say that "The term "biologically functional equivalent" is well understood in the art and is further defined in detail herein as a gene having a sequence essentially as set forth in SEQ ID NO:2 or SEQ ID NO:25, and that is associated with the ability to bind and endocytose at least one of HA, chondroitin and chondroitin sulfate. Thus, while the specification does provide a definition for the term introduced into the claims, the definition is circular, as the terms "essentially as set forth" and "biologically functional equivalent" are used each to define the other. Further, the definition is extremely broad, as it encompasses an unspecified number of substitutions in the disclosed sequence, as long as the resulting protein remains "biologically functionally equivalent."

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The claimed invention is drawn to mammalian HARE, and compositions comprising such. The state of the prior art, as set forth in the previous Office Action, is that both human and rat 175 and 300 kD HARE were known and isolated, but had not been cloned. HARE 175 was known to be a single protein, and HARE 300 was known to be trimeric. No other HARE from other mammalian species have been isolated or characterized, nor had any functional fragments of HARE been described or isolated. The specification as filed provides little guidance as to how the HARE175 might be altered and still retain function. The working examples include the isolation

of both HARE 175 and HARE 300 receptors from natural sources, a complete clone of rat HARE 175, and a partial clone of human HARE 175. There are no working examples of alterations of any HARE receptor. Accordingly, it is concluded that it would require undue experimentation to practice the claimed invention in a manner commensurate in scope with the claims.

The Examiner's position that the disclosure of HARE 175 and one complete and one partial clone encoding it does not enable the scope of all proteins that are biologically functionally equivalent to such is supported by the case law. It was found in Ex parte Maizel (27 USPQ2d 1662 at 1665) that:

> Appellants have not chosen to claim the DNA by what it is but, rather, by what it does, i.e., encoding either a protein exhibiting certain characteristics, or a biologically functional equivalent thereof. Appellants' claims might be analogized to a single means claim of the type disparaged by the Court of Customs and Patent Appeals in In re Hyatt, 708F.2d 712, 218 USPQ 195 (Fed. Cir. 1983). The problem with the phrase "biologically functional equivalent thereof" is that it covers any conceivable means, i.e., cell or DNA, which achieves the stated biological result while the specification discloses, at most, only a specific DNA segment known to the inventor. Clearly the disclosure is not commensurate in scope with the claims."

Although the claims in this case are drawn to protein and not to DNA, the issue is analogous. The phrase "biologically functional equivalent" encompasses any possible protein that shares function with the protein of SEQ ID NO:2, that is, binds at least one of HA, chondroitin, or chondroitin sulfate. As was the case in *Maizel,* clearly enablement is not commensurate in scope with the claims.

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 24, 42 and 88 are rejected under 35 U.S.C. 102(a) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over McCourt et al., Hepatology 30:1276, cited by applicants, or Zhou et al., JBC 274(48):33831-33834, also cited by applicants, for reasons of record with respect to the rejection of claims 19-27 and 41-47 in the previous Office Action.

The rejection over the Zhou et al., JBC 274(48):33831-33834 reference is withdrawn in view of the declaration by Paul Weigel, submitted 2/13/03, which although submitted under 37 C.F.R. § 1.132, is persuasive under 37 C.F.R. § 1.131, in establishing that the work described therein was not by another.

The rejection is maintained over the McCourt reference. Applicants argue in paper number 15, submitted 2/13/03, that because the McCourt reference was *accepted* for publication after the Zhou reference was *received* for publication, that there is demonstration of conception and constructive reduction to practice of the present invention prior to the publication date of the McCourt et al. reference. This argument has been fully considered but is not deemed persuasive as receipt for publication merely denotes when the first draft was submitted. It is not evidence as to

what that first draft contained. It is common in the art for publications to undergo substantial revision between the first submitted draft and the published manuscript, often including additional experimentation. In view of such, the mere date of submission of the first draft cannot be relied upon to establish conception and reduction to practice. Applicants may wish to resolve this issue by submission of an additional declaration under 37 C.F.R. § 1.131 by the inventor, submitting a copy of the manuscript as it was submitted on that date, or alternatively stating that the published version was the same as that submitted on 7/25/99.

Claims 24, 42 and 88 are rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Yannariello-Brown et al., Glycobiology 7:15, cited by applicants, for reasons of record in the previous Office Action at pages 9-10, as applied to claims 19-27 and 41-47.

As stated in the previous Office Action, Yannariello-Brown et al. disclose the purification of rat liver sinusoidal endothelial cell hyaluronan receptor (title). At page 15, first column, they disclose that both 175 kDa and 300 kDa receptors were isolated. See page 18 for discussion of fractions having activity; those fractions meet the limitation of being 'purified mammalian HARE' as they are purified relative to their naturally obtainable state (see page 49 of the specification wherein this definition is set forth), and also of being compositions, as they were not purified to homogeneity.

The Yannariello-Brown reference is silent with respect to amino acid sequence of the isolated receptors and also with respect to binding of particular antibodies thereto. However, in view of the source, properties, and molecular weights of the disclosed receptors, they appear to be consistent with those of the claims. The examiner is unable to determine whether the prior art disclosure possesses the unrecited characteristics or property. With these conditions, where the (product or apparatus or method or product by process) seems to be identical except that the prior art is silent to the characteristic or property claimed, then the burden shifts to applicant to provide evidence that

the prior art would neither anticipate nor render obvious the claimed invention. Note the case law of *In re Best* 195 USPQ 430, 433 (CCPA 1977).

Applicants traversal of this rejection, and the declaration by Paul Weigel regarding this rejection, have both been fully considered but are not deemed persuasive. Both documents argue that the purity of the protein disclosed in the reference is insufficient to meet the claim limitations. However, as stated in the original rejection, and reiterated above,

> See page 18 for discussion of fractions having activity; those fractions meet the limitation of being 'purified mammalian HARE' as they are purified relative to their naturally obtainable state (see page 49 of the specification wherein this definition is set forth), and also of being compositions, as they were not purified to homogeneity.

It remains that the fractions of Yannariello-Brown et al. meet the claim limitations. Applicants have neither amended the claims to define over the reference, nor have they provided evidence to the contrary. The Examiner further notes applicants argument at pages 7-8 of paper number 15 that "even if this sequence were obtainable based on the teachings of the Yannariello-Brown et al. reference, it would only be a small fragment of SEQ ID NO:2....". This argument has been fully considered but is not deemed persuasive because it misses the point of the rejection, which is that the fractions disclosed by Yannariello-Brown et al. inherently possess the sequence of SEQ ID NO:2. It is not necessary that Yannariello-Brown's protein have been pure enough to sequence, as there is no such limitation in the claims, nor have applicants provided any facts or evidence to support the assertion that only a small fragment of SEQ ID NO:2 would be so obtained. Accordingly, the claims remain anticipated or obvious over the disclosure of Yannariello-Brown et al.

Advisory Information:

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228.

Lorraine Spector, Ph.D.
Primary Examiner

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4/23/03